REMARKS

Claims 1 through 17 are presently in the subject application.

Claims 1-6 and 9-17 are rejected under 35 U.S.C. § 103(a) as obvious over Whitcomb, U.S. Patent No. 6,011,049 ("WHITCOMB"). It is respectfully submitted that WHITCOMB does not render Applicants' **core** formulation obvious .

Certainly, as the Examiner points out, WHITCOMB reveals combining pioglitazone plus metformin. However, WHITCOMB does not reveal the novel and patentable delivery system as defined by Applicants in claims 1-6 and 9-17. All that WHITCOMB reveals are conventional delivery systems, e.g., tablets, capsules, etc. In this regard, reference is made to WHITCOMB at col. 4, lines 35-41, where it is stated,

> The compounds can be employed individually, or can be combined in a single formulation, for example as a tablet, capsule, syrup, solution, as well as controlled release formulations. In a preferred embodiment, the sulfonylurea biguanide, and glitazone are **formulated individually** and administered in the same manner that each is **normally used** clinically. (emphasis added);

and at Col. 5, lines 28-33, where it is stated:

> ... The compositions will normally be made for oral administration, for instance as tablets or capsules, but also may be in the form of aqueous suspensions or solutions, suppositories, slow release forms, for example employing an osmotic pump, skin patch, or the like.

What was not appreciated by WHITCOMB was a consideration of the relative concentrations of each drug, the dose requirement of pioglitazone vis-a-vis metformin, and the comparative solubility rates and absorption rates of each drug. In this regard, reference is made

to the subject specification, at page 3, first through fourth full paragraphs, and in particular, the first full paragraph, where it is stated:

> ... The first layer [of the defined **core** formulation] should comprise pioglitazone hydrochloride because its dose requirement is lower compared to metformin. Additionally, it is slightly non-polar, its solubility rate slower, and its absorption rate thus dependent on its dissolution rate in the contents of the gastrointestinal tract compared with metformin.

Merely admixing two or three medicaments, as disclosed in WHITCOMB, does not address the considerations which Applicants' core formulation and method using such formulation addresses.

The Examiner states,

> The combined ... may take the form of a tablet. One would know that in the formation of the tablet, the ingredients would be compressed together, thereby allowing a portion of metformin to be covered with pioglitazone, i.e., forming a core and a first layer.

It is respectfully submitted that one of ordinary skill in the art would not know of this formation. This is pure conjecture on the part of the Examiner without any support. As stated by the CCPA in *In re Way*, 514 F.2d 1057, 185 USPQ 580, 584 (CCPA 1973),

> There is no support for [the solicitor's] analogy from the technical literature and a fertile imagination does not make the claimed invention obvious.

Additionally, reference is made to *In re GPAC* 57 F.3d 1573, 35 USPQ 2d 1116, 1123 (Fed. Cir. 1995), where the CAFC stated:

> We believe that this statement by the Board in support of its rejection ... is conclusory and lacks the factual basis required to validate a claim rejection under section 103. See *In re Warner*, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967) "A rejection

> based on Section 103 must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art.... [The Board] may not ... resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis") *cert denied*, 389 U.S. 1057 (1968).

Arguendo, it can just as easily be forwarded that (1) separate medicament layers are formed; or (2) a mixed active ingredient core is formed with a metformin layer covering it; or (3) a metformin core is formed with a pioglitazone layer; or (4) a mixture of different discrete cores, are formed, etc. But, what is realistic?

Of course, one of ordinary skill in the art knows the difference between a coated particle and a core (the central, foundational part of a body or unit) having a layer thereon.

It is respectfully submitted that claims 1-6 and 9-17 are not rendered obvious under 35 U.S.C. § 103(a) in view of WHITCOMB and allowance of these claims is requested.

Claims 1-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rievely, U.S. Patent No. 6,153,632 ("RIEVELEY"). It is respectfully submitted that RIEVELEY does not render claims 1-17 obvious under 35 U.S.C. § 103(a) and allowance of these claims is requested.

All that RIEVELEY reveals is a combination of a glitazone e.g., pioglitazone, and a biguanide, e.g. metformin. RIEVELEY does not reveal the core formulation as defined by Applicants. All that RIEVELEY reveals are conventional delivery vehicles. In this regard, reference is made to RIEVELEY at col. 6, lines 41-61, where it is stated:

> The subject compositions ... can be administered parentally, topically or internally, but preferably orally ... The compositions ... may be formulated in any suitable orally acceptable form by employing **conventional**

> formulation techniques ... in pharmaceutically acceptable forms such as tablets or capsules in **admixture** with ... carriers.... may also be used in **combination** with other ... agents ... may be formulated in one unit ... or in separate units administered at the same time or at separate times ... administered in a single dosage form or in the form of subunits several times a day. (emphasis added).

The Examiner has stated:

> As above, Rieveley does not explicitly state the use of pioglitazone HCI in the first layer and a biguanide at the core ... but because there is **no evidence of criticality** in such Applicant's formulation, the instant invention is made obvious by Rieveley (emphasis added).

As shown above, Applicants have shown a criticality. As with WHITCOMB, reference is made to the subject specification at page 3, first through fourth paragraphs, especially the first full paragraph. Again, merely combining or admixing two or three medicaments does not address the problems or considerations addressed by Applicants'invention as defined in claims 1-17.

It is respectfully submitted that claims 1-17 are not rendered obvious under 35 U.S.C. § 103(a) in view of RIEVELEY and allowance of claims 1-17 is requested.

Pursuant to the provisions of §§1.56, 1.97, and 1.98 of Title 37 of the Code of Federal Regulations, as amended, applicants hereby cite to the United States Patent and Trademark Office the following:

1. U.S. Patent No. 6,197,340 B1, granted to Edward A. Byrd et al. on March 6, 2001

Copies of the patents compiled herein are submitted herewith.

Applicants respectfully request the Examiner in charge of the above-captioned application to consider the aforelisted patent in connection with the examination of the application and to cite those deemed to be material to the determination of patentability.

Applicants respectfully submit that the aforelisted patent, does not, alone or in combination, anticipate or render obvious the subject matter of the present application.

For the convenience of the U. S. Patent and Trademark Office, applicants submit herewith Form PTO-1449 listing the patents cited herein.

A check in the amount of $ 180.00 is enclosed herewith pursuant to 37 CFR 1.17(p).

Please charge any additional fees required or credit any overpayment to Deposit Account No. 50-0320.

The Examiner is hereby authorized to call the undersigned attorney of record "collect' on any matter connected with this application. The telephone number is 212-588-0800. In the absence of the undersigned attorney of record, the call will be accepted by any attorney empowered in this application.

Respectfully submitted,

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